REMARKS

The above amendments to the above-captioned application along with the following remarks are being submitted as a full and complete response to the Office Action dated August 19, 2004 and the phone interview with the Examiner on November 16, 2004. Applicants thanks the Examiner for taking the time to conduct the phone interview. The Examiner indicated that the response addressed the outstanding 112 and 102, 103 issues but requires an updated prior art search.

In view of the above amendments and the following remarks, the Examiner is respectfully requested to give due reconsideration to this application, to indicate the allowability of the claims, and to pass this case to issue.

Status of the Claims

Claims 1-9 are pending in this application. Claims 1-3, 5 and 8 are being amended to more particularly point out and distinctly claim the subject invention. A new claim 9 is being added to recite other embodiments described in the specification. Applicant hereby submits that no new matter is being introduced into the application through the submission of this response.

Formality Rejection

Claims 1-8 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite, for the recitation of "visually-intuitive graphical representation". As indicated, the claims have been amended as required by the Examiner. Accordingly, the withdrawal of the outstanding informality rejection is in order, and is therefore respectfully solicited.

Prior Art Rejections

Claims 1-6 and 8 were rejected under 35 U.S.C. § 102(b) as being anticipated by an article by Eisen et al. published on PNAS, vol. 95, pp. 14863-14868, Dec. 1998 (hereinafter "Eisen"), and claim 7 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Eisen in view of an article by Lockhart published on Nature Biotechnology. Vol. 14, pp. 11675-1680 1996 (hereinafter "Lockhart"). Claim 1 was rejected under 35 U.S.C. §102(b) as being anticipated by Lockhart, and claims 2 to 7 were rejected under 35 U.S.C. §103(a) as being

unpatentable over Lockhart, in view of U.S. Patent No. 6,528,264 to Pal et al. (hereinafter "Pal"). These rejections have been carefully considered, but are most respectfully traversed.

The present invention as now claimed is directed to a method for displaying results of a hybridization experiment in which a plurality of probe biopolymers *immobilized* on a biochip" p. 6, lines 7-8) are hybridized to a sample biopolymer. The method incorporates the steps of determining information obtained in the hybridization experiment about a hybridization level for each of the probe biopolymers; determining a probe ***homologous*** similarity score(e.g., Fig. 7; p. 13, lines 19-24), which represents a homologous similarity between first probe data 301 (e.g., Fig. 5 including probe ID, name, definition, sequence, etc) on a base sequence of at least one of the probe biopolymers and second probe data on a base sequence of at least one other of the probe biopolymers, according to an algorithm for calculating degrees of homology between two biopolymer sequence (e.g., Smith-Waterman method, BLAST, or the like (p. 3, lines 7 and 11); "*Many other algorithms have been developed for the same purpose. In these approaches, the degrees of homology between two DNA sequences are expressed by indices such as "homology score," ... or by "matching rate,"*" p. 3, lines 7-23); and displaying (1) the information about the ***hybridization*** level (e.g., 705 in Fig. 12; 807 in Figs. 13-14) for each of the probe biopolymers together with (2) the probe homologous similarity score (808 in Figs. 13-14), including generating a visual graphical representation of the determined hybridization level and correspondingly determined probe homologous similarity score (e.g., Fig. 18) so as to provide at least one of a visual confirmation of similarities between the base sequences of corresponding biopolymers used in the hybridization experiment and a visual indication of unexpected or improper hybridization.

Taking Fig. 16 as an example, a framed portion 809 in the hybridization-level data 807 indicates that the hybridization level of Probe 1 is very close to that of Probe 2 in Chip 2. A framed portion 810 in the probe homologous similarity score pattern 808 confirms that the sequences of the DNA probes, Probe 1 and Probe 2, are in fact very homology similar to one another (p. 17, last paragraph). Taking Fig. 18 as another example, the probe homologous similarity score pattern matrix 901 shows that Probe 1 and Probe 2 have very similar physical DNA sequences, but the tree diagram 1001 indicates that the probes have rather different homologous properties from one another (Probe 1 is more closely related to Probe 4). Regarding Fig. 18, although both the hybridization-level data and the probe homologous

similarity score pattern matrix 901 show that Probe 1 and Probe 2 have very similar physical DNA sequences, but the tree diagram 1001 indicates that the probes have rather different homologous properties from one another (Probe 1 is more closely related to Probe 4). The hybridization-level data reflect the physical similarity of the DNA probes 1 & 2, while the probe homologous similarity score may be partially influenced by their physical similarity, rather than only reflects their homologous similarity (p. 19, last paragraph). In other words, the sample DNA molecules of the same type bind to two different types of DNA probes 1 & 2 that are physically very similar to one another, i.e., unintended hybridization or miss-hybridization(p. 2, lines 12-17). Accordingly, the invention "*determines if unintended hybridization has occurred by observing the hybridization-level information in the proximity of the object probe. Also, by selecting the information to be displayed with the similarity score matrix, the verification of the accuracy of the hybridization is possible in wider ranges* (p. 8, lines 4-9)".

Applicants respectfully contend that neither Eisen, nor Lockhart teaches or suggests at least "determining a **probe homologous similarity** score according to an algorithm for calculating degrees of homology between two biopolymer sequences" and then "displaying said information about the hybridization level for each of the probe biopolymers together with said probe homologous similarity score" so as to provide a visual indication of unexpected or improper hybridization according to the invention.

In contrast, Eisen's yeast expression analysis (same as P. Brown's group of the Stanford University referenced on p. 4 line 3 of the specification) merely (i) clusters probes so as to display (Fig. 1) a cluster tree diagram (p. 14863, right col. 2nd paragraph) and (ii) indicates a hybridization level between a probe ***A*** and a sample ***B*** (*probe vs. sample* p. 4, lines 2-18), but not calculates according to an algorithm for calculating degrees of homology between two biopolymer sequence to obtain "probe homologous similarity scores" which reflect homologous similarity between any two probes (*probe vs. probe*). "*No practical approach is known for determining if a probe biopolymer has been accurately hybridized to a sample biopolymer of interest, and accordingly, there is a need for such a method* (p.4, lines 19-22)." Eisen simply does not provide a visual indication of unexpected or improper hybridization. The invention is specifically directed to displaying the probe homologous similarity score along with and hybridization-level data are displayed side-by-side so to be compared with each other in a manner that is visually easy to understand (p. 5, lines 5-11).

The probe homologous similarity score is represented by square patterns having varying color depths (rather than any cluster tree), so as to make the displayed image, and consequently the information being represented, more visually intuitive (p. 6, lines 14-19).

Lockhart merely quantitatively relates hybridization intensities of mRNAs, i.e., samples, to arrays of synthetic oligonucleotides, i.e., probes (*sample vs. probe* p. 1675, left col., lines 5-8; "*RNA concentration*" Fig. 3; "*A total of 21 murine RNAs were detected at levels ranging from approximately 1:300,000 to 1:100.*" Fig. 5), rather than calculating any "probe homologous similarity score" between the probes immobilized on a biochip (*probe vs. probe*) and then displaying the score along with the hybridization levels as the present invention.

Pal was relied upon by the Examiner to teach displaying intensity of signals with color differentiation and comparing different biochips. However, Pal fails to compensate for Lockhart's deficiencies since Pal does not disclose, teach or suggest calculating and displaying the "***probe homologous similarity*** score" along with the hybridization levels as the present invention.

Neither Lockhart nor Pal discloses, teaches or suggests the generating of a visually-intuitive graphical representation of the determined hybridization level and correspondingly determined probe homologous similarity score to show unexpected or improper hybridization. The combination of these references would fall short of embodying a method having every feature of the present invention as claimed, most especially the features as noted above.

Further, since claims 2 - 7 recite features in addition to those in independent claim 1 that are already not shown by the cited prior art, these same references cannot be used to render obvious the more specific features of dependent claims 2 - 7. Rather, the present invention as a whole is distinguishable and thereby allowable over the prior art.

Although the invention applies general homology analysis, such as Smith-Waterman method or BLAST (p. 3, lines 7 and 11), the invention applies the homology analysis between probes rather than between a probe and a sample and then displays the "*probe homologous similarity score*" along with the hybridization levels to achieve unexpected results or properties. For example, determining if unintended hybridization occurs (Fig. 18). The presence of the unexpected properties is evidence of nonobviousness. MPEP§716.02(a).

> *"Presence of a property not possessed by the prior art is evidence of nonobviousness. In re Papesch, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) (rejection of claims to compound structurally similar to the prior art compound was reversed because claimed compound unexpectedly possessed anti-inflammatory properties not possessed by the prior art compound); Ex parte Thumm, 132 USPQ 66 (Bd. App. 1961) (Appellant showed that the claimed range of ethylene diamine was effective for the purpose of producing " 'regenerated cellulose consisting substantially entirely of skin' " whereas the prior art warned "this compound has 'practically no effect.' ").*

Although "[t]*he submission of evidence that a new product possesses unexpected properties does not necessarily require a conclusion that the claimed invention is nonobvious. In re Payne, 606 F.2d 303, 203 USPQ 245 (CCPA 1979). See the discussion of latent properties and additional advantages in MPEP § 2145*," , the unexpected properties were unknown and non-inherent functions in view of Brown or Lockhart, since they do not inherently achieve the same results. In other words, these advantages would not flow naturally from following their teachings, since Brown and Lockhart fail to suggest applying homology analysis among probes thereby determining and displaying probe homologous similarity scores.

Applicants further contend that the mere fact that one of skill in the art could apply homology analysis from 'between a sample and a probe' to 'between two probes' to meet the terms of the claims is not by itself sufficient to support a finding of obviousness. The prior art must provide a motivation or reason for one skilled in the art to provide the unexpected properties, such as determining a probe homologous similarity score thereby determining if unintended hybridization occurs, without the benefit of appellant's specification, to make the necessary changes in the reference device. *Ex parte Chicago Rawhide Mfg. Co.*, 223 USPQ 351, 353 (Bd. Pat. App. & Inter. 1984). MPEP§2144.04 VI C.

Applicants contend that neither Brown, Lockhart, Pal, nor their combination teaches or discloses each and every feature of the present invention as disclosed in independent claim 1. As such, the present invention as now claimed is distinguishable and thereby allowable over the rejections raised in the Office Action. The withdrawal of the outstanding prior art rejections is in order, and is respectfully solicited.

CONCLUSION

In view of all the above, Applicant respectfully submits that certain clear and distinct differences as discussed exist between the present invention as now claimed and the prior art references upon which the rejections in the Office Action rely. These differences are more than sufficient that the present invention as now claimed would not have been anticipated nor rendered obvious given the prior art. Rather, the present invention as a whole is distinguishable, and thereby allowable over the prior art.

Favorable reconsideration of this application as amended is respectfully solicited. Should there be any outstanding issues requiring discussion that would further the prosecution and allowance of the above-captioned application, the Examiner is invited to contact the Applicant's undersigned representative at the address and phone number indicated below.

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November 18, 2004

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